REMARKS

Status of the Claims

Responsive to the Restriction Requirement mailed April 22, 2003, claims 5-12 have been canceled without prejudice to or disclaimer of the subject matter therein. Claim 1 has been amended to recite "An isolated nucleic acid comprising a polynucleotide having at least 80% sequence identity to SEQ ID NO:1...." Support for the amendment can be found in the specification at page 28, line 24. Therefore, no new matter has been added by amendment.

Claims 1-4 and 13-17 are now pending. The Examiner's comments are addressed below in the order set forth in the Office Action.

Objection to the Specification

The Examiner objects to the specification for containing embedded hyperlinks. Responsive to the Examiner's objection, the specification has been amended to remove the "www" required to embed the link, thereby obviating the objection.

Objection to the Claims

Per the Examiner's suggestion, claim 3 has been amended to recite "the," thereby obviating the objection. Applicant wishes to thank the Examiner for the helpful suggestion.

The Rejections of the Claims under 35 U.S.C. § 101 Should Be Withdrawn

Claims 1-4 and 13-17 stand rejected under 35 U.S.C. § 101. These rejections are respectfully traversed.

The Office Action alleges that Applicant's invention does not meet the utility guidelines. In particular, the Office Action asserts that the predicted function is based solely upon sequence comparison with an antifungal protein from a fly; that no antifungal domain or data relating the claimed sequences to antifungal proteins has been disclosed;

and that the working example does not establish antifungal activity. These statements mischaracterize Applicant's disclosure.

First, Applicant's claimed sequences encode *defense inducible proteins*. Furthermore, the assertion in the Office Action that function was assigned based solely upon sequence homology is not accurate. Function was actually assigned based upon the sequences high representation in cDNA derived from leaf tissue resistant to fungal infection or from leaf tissue treated with jasmonic acid (a chemical elicitor of plant defense responses). Although homology was observed between these sequences and the antifungal protein of Iijima *et al.* (1993) *J. Biol. Chem.* 268:12055-61, the functional characterization of Applicant's defense inducible protein was *not* based solely upon sequence homology. Consequently, the Office Action's statement that no antifungal domain has been disclosed is not relevant to the utility inquiry.

Moreover, the expression data presented in Applicant's working example does support a conclusion that Applicant's claimed sequences are *defense inducible proteins*. As is well known in the art, defense inducible proteins need not possess *direct* antipathogen activity. See WALTON, "Biochemical Plant Pathology," *Plant Biochemistry*, 1997, pp. 496-502, Academic Press, San Diego (describing induced resistance in plants). As Walton describes, some proteins induced by pathogens do possess direct antimicrobial enzymatic activity (such as chitinases, etc.), but others don't. Such sequences have art-recognized utilities, for instance, in the creation of transgenic plants with enhanced disease resistance.

Nonetheless, the Office Action rejects the claims on the grounds that sequence homology is insufficient to establish utility. In support, the Office Action cites Bork *et al.* (2000) *Genome Research* 10:398-400 and Lacombe *et al.* (2001) *Science* 292:1486-7. Applicants disagree with this premise. For instance, Table 1 of Bork gives the prediction accuracy for functional features based on sequence homology as 90%, suggesting that such predictions are, in fact, quite reliable. The reference goes on to suggest the error rate in predictions of function based on sequence similarity can be reduced even further

by using complementary sources of information (see page 399, column 3 to page 400, column 1). In any case, neither Bork nor Lacombe *et al.* are applicable to the present application because function was *not* assigned based upon homology alone.

The Office Action suggests that if direct antifungal activity were disclosed, the claimed sequences would be accorded utility. It is not the applicant's burden to establish utility, however, unless the Examiner shifts the burden by establishing, with evidence, that one of skill in the art would doubt the asserted utility. *In re Brana*, 34 U.S.P.Q.2d 1437, 1441 (Fed. Cir. 1995)("Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the Applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility."). The Office Action has not met this burden because the rejection incorrectly assumes that utility is founded upon sequence homology alone.

Further, the Federal Circuit has emphasized that "a 'rigorous correlation' need not be shown in order to establish practical utility; 'reasonable correlation' is sufficient." *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1565, 39 USPQ2d 1895, 1900 (Fed. Cir. 1996). Utility for the present sequences is supported by the high levels at which these sequences are expressed in leaf tissue resistant to fungal infection or leaf tissue treated with jasmonic acid. Those of skill in the art recognize such expression data as a scientifically valid basis for identifying genes involved in plant defense. See, e.g., Xiong *et al.* (2001) "Identification of defense-related rice genes by suppression subtractive hybridization and differential screening," *Mol. Plant Microbe Interact.* 14:685-92. Such genes are utilized by those of skill in the art to create transgenic plants with enhanced disease resistance. Accordingly, there is a reasonable correlation between the utility for the present invention and Applicant's expression data. This is sufficient to meet the statutory standard for utility.

In summary, the Office Action's assertion that utility for the claimed sequences has been based upon homology alone is incorrect. Further, the data presented by Applicant meets the statutory standard for utility for each of the claimed sequences.

Accordingly, the rejection of the claims 1-4 and 13-17 under Section 101 should be withdrawn and should not be applied to the amended claims.

The Rejections of the Claims under 35 U.S.C. § 112, First Paragraph Should Be Withdrawn

Claims 1-4 and 13-17 stand rejected under 35 U.S.C. § 112, first paragraph, enablement. The rejection of these claims is respectfully traversed.

The Office Action asserts that one of skill in the art would not be able to use the present invention. In particular, the Office Action states that Applicant has assigned a function to the claimed sequences solely based on sequence homology. To the contrary, the asserted function is based on their expression in resistant tissue or tissue treated with a well-known defense response elicitor, not solely upon sequence homology. As evidenced by Xiong *et al.* (2001) *Mol. Plant Microbe Interact.* 14:685-92, those of skill in the art utilize such data to identify defense related genes. The Office Action also states that Applicant has not demonstrated direct antifungal activity for the claimed sequences. However, it is recognized in the art that not all defense related proteins demonstrate *direct* antimicrobial activity. See WALTON, "Biochemical Plant Pathology," *Plant Biochemistry*, 1997, pp. 496-502, Academic Press, San Diego (describing induced resistance in plants). Neither of the Office Action's statements demonstrate that one of skill in the art would fail to understand how to use the claimed sequences.

The Office Action also asserts that Applicant's sequences do not satisfy the criteria described in van Loon *et al.* (1999) *Phys. Mol. Plant Pathology* 55:85-97 for establishing a new family of pathogenesis-related proteins. These criteria are arbitrary standards suggested by van Loon for establishing new family of pathogenesis-related proteins in tobacco and tomato. There is no indication that the criteria is widely accepted or currently used. Notably, Walton makes no mention of such criteria in his review of induced resistance in plants. In any case, the Federal Circuit has cautioned against applying standards other than those required by Section 101 and 112 of the patent statute.

In re Brana, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995)(overturning the PTO's Section 112 rejection on the grounds that an incorrectly rigorous standard had been applied).

Under Section 112, first paragraph, the enablement standard is satisfied if one of skill in the art can make and use the claimed invention without undue experimentation. Applicant has disclosed novel nucleic acids encoding defense inducible proteins. These sequences are highly expressed in leaf tissue resistant to fungal inoculation. See Example 3. The specification teaches that these sequences are utilized to generate transgenic plants. See the specification, page 2, lines 11-13. Techniques for the generation of transgenic plants are set forth in the specification at pages 54, line 6 to page 55, line 27 and, further, are known in the art. Transgenic plants expressing these sequences can be screened for disease resistance using the techniques described in the specification on page 22, lines 4-29. Similar techniques are known in the art. The present sequences can also be used in a breeding program to identify plants possessing constitutive, hereditary disease resistance. See the specification, page 23, lines 29-30. In another embodiment, the present sequences can be operably linked to a plant promoter under environmental control, such as a pathogen- or wound-inducible promoter. Guidance for carrying out these methods is provided in the specification at pages 42-43 and, further, are known in the art.

The Federal Circuit has held that claims are enabled where steps of the claimed method required the use of molecular biology techniques and a screening test for functionality. *See Ajinomoto Co. v. Archer-Daniels-Midland Co.* (56 USPQ2d 1332, 228 F.3d 1338 (Fed. Cir. 2000), *reh'g en banc denied* Nov. 14, 2000). In finding that the claims were enabled, the court noted that "all of the methods needed to practice the invention were well known to those skilled in the art" and that "the process used conventional and well-known genetic engineering techniques." 56 USPQ2d at 1337, 228 F.3d at 1345. The present disclosure meets this standard and the rejection of claims 1-4 and 13-17 under Section 112, first paragraph, enablement, should be withdrawn and should not be applied to the amended claims.

The Office Action further rejects claims drawn to "polynucleotides having at least 75% sequence identity" to the sequences of the invention. Presumably, this rejection applies only to claims 1-4. Applicant traverses. However, in the interest of expediting prosecution, Applicant has amended claim 1 to recite "An isolated nucleic acid comprising a polynucleotide having at least 80% sequence identity to SEQ ID NO:1...." The rejection should not be applied to the claims as amended.

The Office Action acknowledges that such sequences can be generated by standard mutagenesis techniques but asserts that "it is unpredictable if any polynucleotide sequence having at least 75% [identity] to SEQ ID NO:1 would encode a maize AFP1 protein" and "that Applicant has not provided guidance for the antisense of SEQ ID NO:1." As discussed above, claim 1 has been amended to recite "An isolated nucleic acid comprising a polynucleotide having at least 80% sequence identity to SEQ ID NO:1...."

Furthermore, guidance for the generation and use of sequences falling within this genus is provided. For instance, guidance is provided regarding conservatively modified sequences is provided in the present disclosure. See the specification, page 5, line 17 to page 6, line 24. By reference to a standard codon table, one of skill in the art could predict which modifications would be tolerated. Further, Applicant has disclosed numerous AFP1 sequences with varying degrees of similarity one to another. Methods for their alignment using the CLUSTAL algorithm are described in the specification at page 16, line 12. By aligning these sequences, one of skill in the art can determine conserved regions unlikely to tolerate mutation. As an illustrative example, Applicant includes an alignment between the nucleotide sequences set forth in the sequence listing as **Exhibit A**. Applicant also submits an alignment between each of the polypeptide sequences set forth in the sequence listing as **Exhibit B**. With respect to the comment regarding antisense, Applicant notes that the specification contains guidance for modulating expression of the present sequences by utilizing an expression cassette

containing an antisense sequence. See the specification, page 46, lines 15-25 and page 58, lines 5-27.

The Office Action also cites Broun *et al.* (1998) *Science* 282:131-133 and Lazar *et al.* (1988) *Molecular and Cellular Biology* 8:1247-1252 for support of the present rejection. However, each reference simply teaches that alteration of highly conserved sequences will disrupt function. For instance, the study of Broun *et al.* targeted amino acid positions that were strictly conserved among the oleate desaturases from *Arabidopsis, Zea mays, Glycine max, R. communis, and Brassica napus*, page 131, column 2, lines 26-31, and it was these conserved residues that were controlling of function. The reference does not support the Office Action's conclusion that most changes are likely to abolish function, as it simply teaches that the alteration of a sequence having a critical role in enzyme activity will disrupt activity of the polypeptide. Lazar *et al.* teach that alterations in amino acid residues 47 and 48 can alter the activity of the TGF-alpha polypeptide. Again, contrary to the conclusion of the Office Action, the alteration in the polypeptide was specifically designed to occur at amino acid positions that are highly conserved in the EGF-like family of polypeptides. As described above, Applicant has disclosed numerous sequences from which information relating to conserved regions can be obtained and has provided guidance within the specification for modifications likely to result in the conservation of function.

The Office Action also cites *In re Wands* and *Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd.* The cases discuss the appropriate standard for determining whether undue experimentation would be required to make and use an invention is discussed. *In re Wands* sets forth the "Wands factors," which are used by courts to assess whether experimentation is "undue." *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Applicants emphasize that it is now customary in the art to make a number of sequences and to test them in a large-scale assay for a desired function and that therefore, such experimentation is not "undue." For example, routine experiments involve what is commonly referred to as "shuffling," as described for example in U.S. Patent No.

5,837,458, issued November 17, 1998 with inventors Minshull and Stemmer and entitled, "Methods and Compositions for Metabolic and Cellular Engineering." The art contains many examples of the use of such techniques. Thus, other publications such as Minshull and Stemmer (1999) *Current Opinion in Chemical Biology* 3:284-290 and Christians *et al.* (1999) *Nature Biotechnology* 17: 259-264 demonstrate that experiments comprising shuffling and large-scale functionality assays are now considered routine in the art. Because such experiments are routine, they would not be considered "undue experimentation" under the *Wands* factors. This is especially so in the present case given the guidance one of skill in the art can gain by aligning the disclosed sequences.

For all of these reasons, the practice of the claimed subject matter does not require undue experimentation. The present rejection under Section 112, first paragraph, enablement, should be withdrawn and should not be applied to the claims as amended.

The Rejections Under 35 U.S.C. § 112, First Paragraph, Written Description, Should be Withdrawn

Claims 1-4 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of an adequate written description. This rejection is respectfully traversed. However, as described above, Applicant has amended claim 1 to recite "An isolated nucleic acid comprising a polynucleotide having at least 80% sequence identity to SEQ ID NO:1...." Claims 2-4 depend from claim 1. The rejection should not be applied to the claims as amended.

A written description can be by structure, formula, chemical name, or physical properties. *See Ex parte Maizel*, 27 USPQ2d 1662, 1669 (B.P.A.I. 1992), *citing Amgen v. Chugai*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). A genus of DNAs may therefore be described by means of a recitation of a representative number of DNAs, defined by nucleotide sequence, falling within the scope of the genus, *or* by means of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559,

1569 (Fed. Cir. 1997); *see also* Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (2001). Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. 66 Fed. Reg. 1099, 1106 (2001). Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. 66 Fed. Reg. 1099, 1106 (2001).

The Office Action concludes that there is no predictable structure encompassed by the sequences claimed within this genus. However, the recitation of at least 80% sequence identity is a *very predictable structure* of the sequences encompassed by the claimed invention. Further, Applicant has disclosed three sequences (SEQ ID NOS:1, 3, and 5), each of which constitutes a representative species. The predictability of the present genus is underscored when one considers an alignment of the polypeptide sequences encoded by each representative species. See **Exhibit C**, which sets forth an illustrative alignment between SEQ ID NOS:2, 4, and 6.

Given the knowledge and level of skill in the art, a person of ordinary skill to envision the claimed invention, *i.e.*, a sequence having at least 80% sequence identity to the sequence set forth in SEQ ID NO:1. Accordingly, the rejection of claims 1-4 under 35 U.S.C. §112, first paragraph, for lack of written description should be withdrawn and should not be applied to the claims as amended.

CONCLUSION

In view of the aforementioned amendments and remarks, Applicant respectfully submits that the objections and the rejections of the claims under 35 U.S. C. §§ 101 and 112 are overcome. Accordingly, Applicant submits that this application is now in condition for allowance. Early notice to this effect is solicited.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR §1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,

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CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Non-Fee Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on October 29, 2003

Nora C. Martinez

Results:

Alignment of all the sequences (blue text represents nucleotide positions conserved among most of the sequences; red text represents nucleotid positions conserved among all of the sequences):

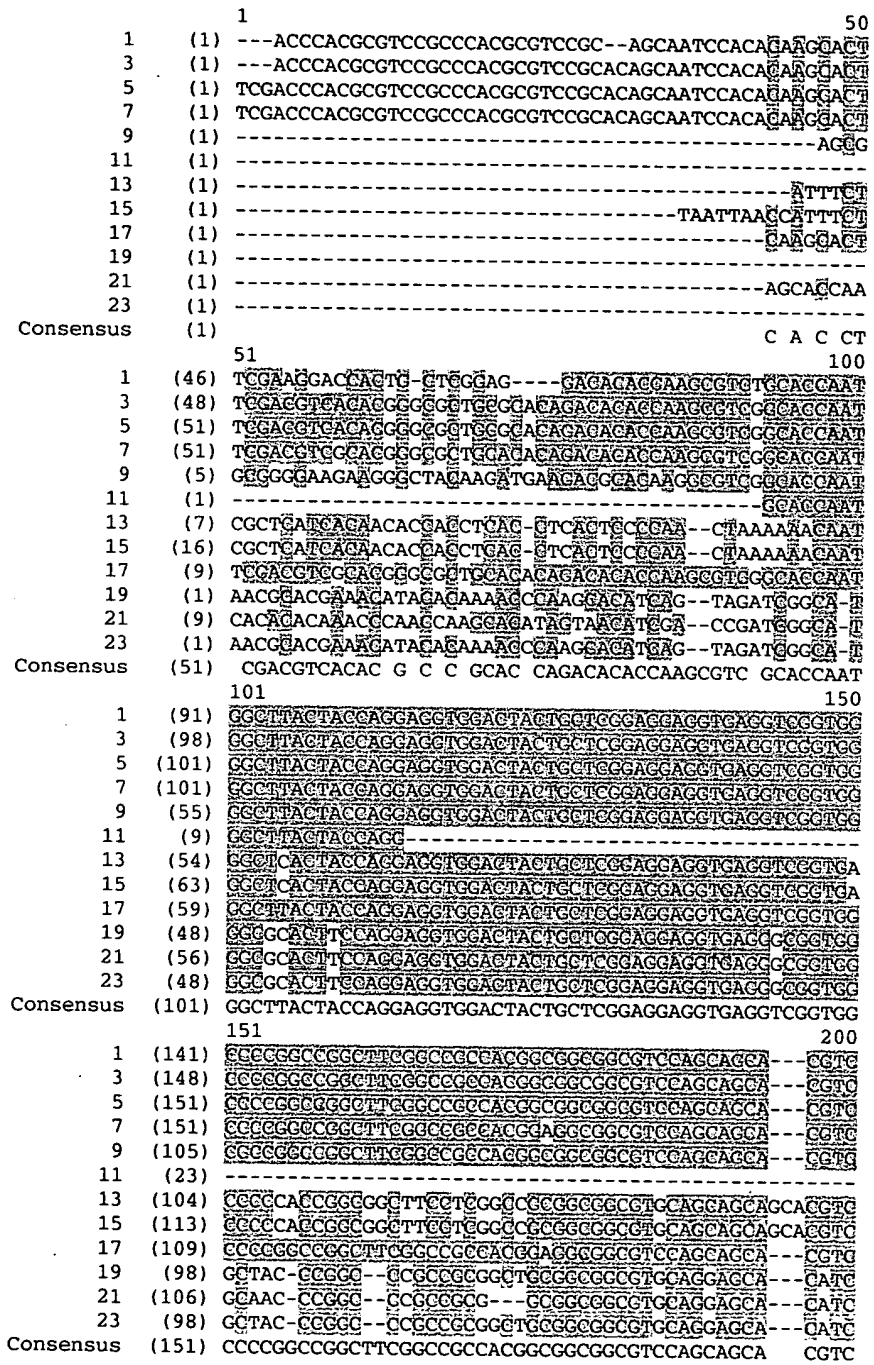

Exhibit A: Alignment of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23

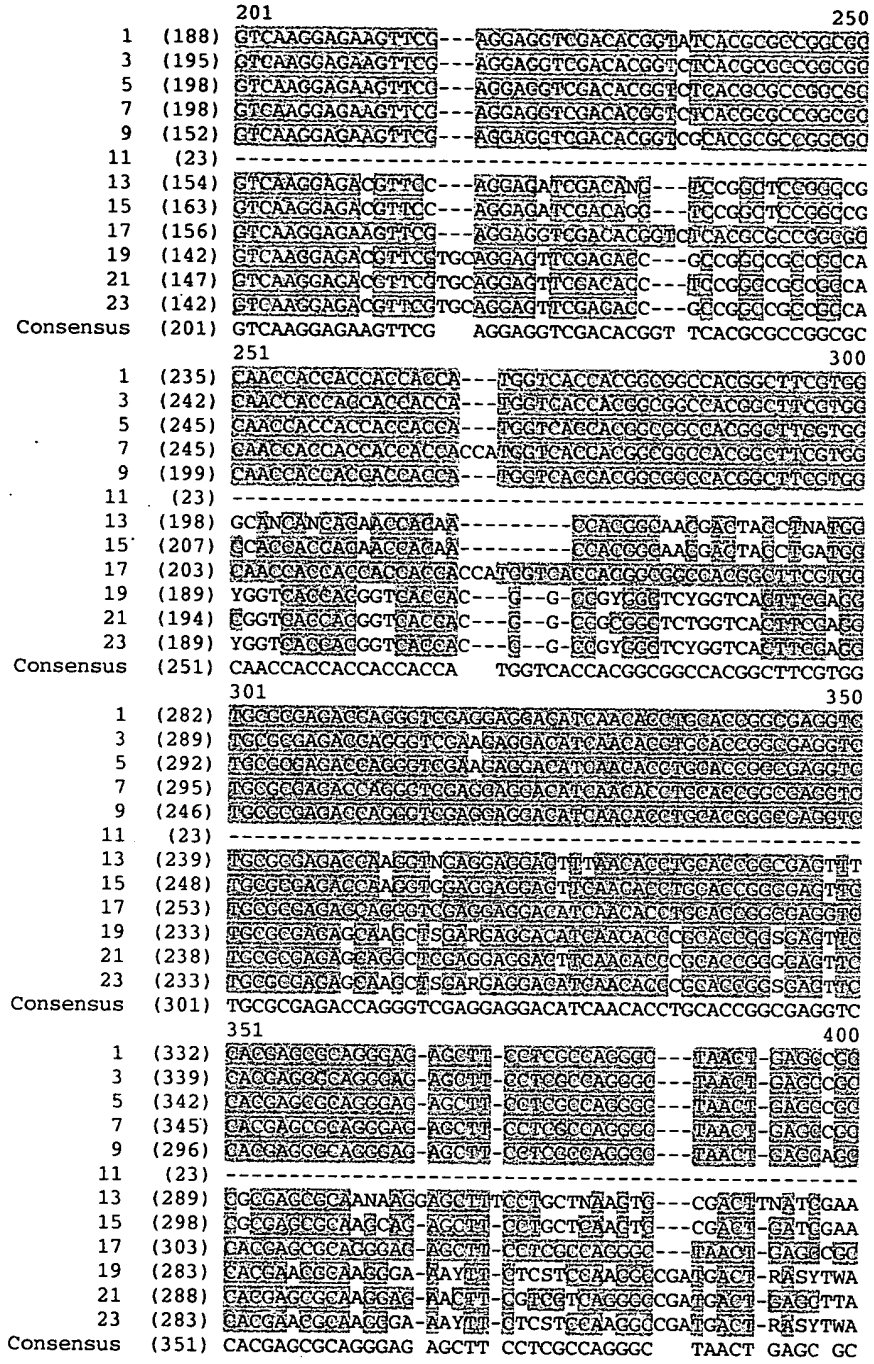

Exhibit A: Alignment of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23

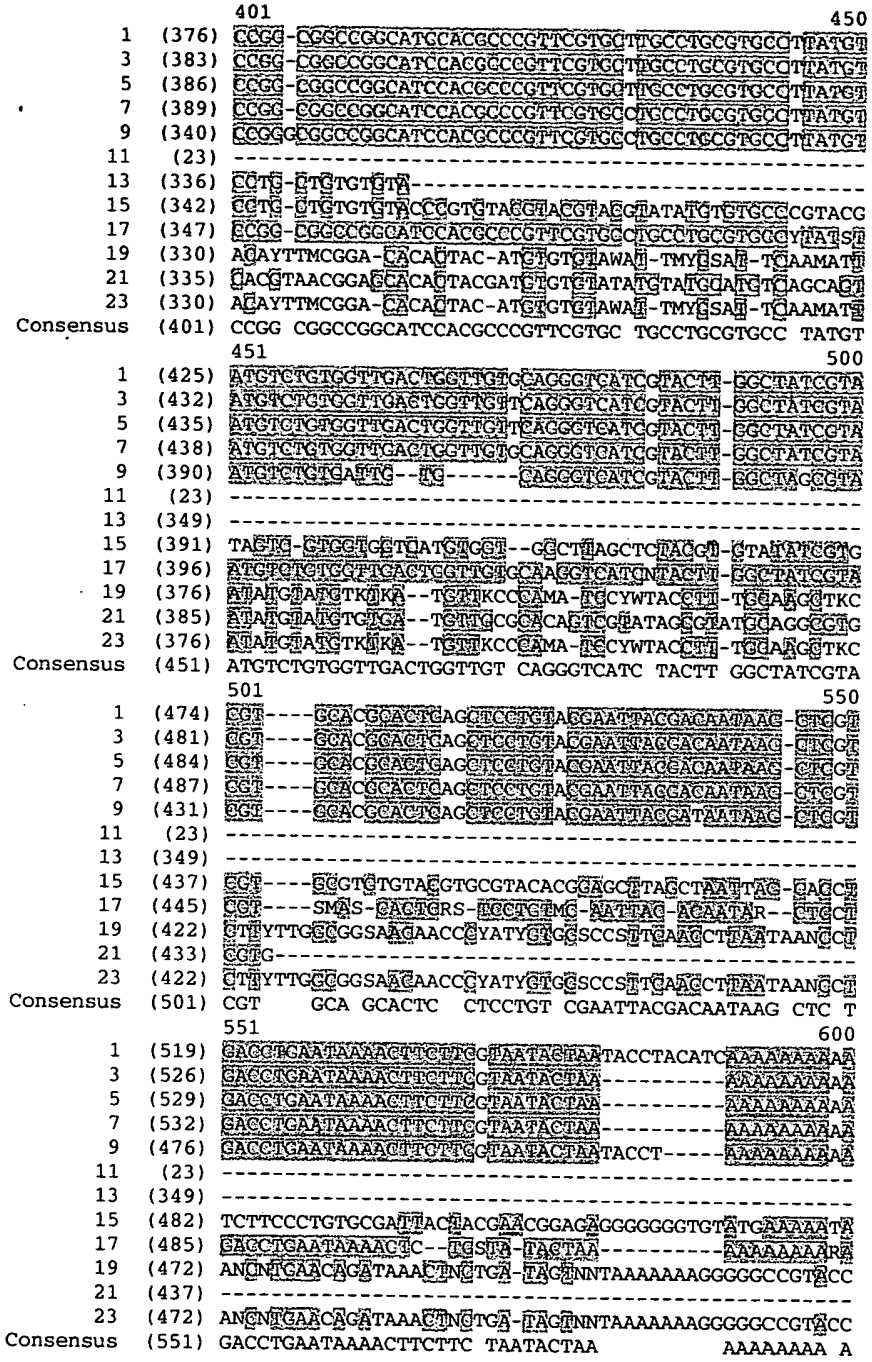

Exhibit A: Alignment of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23

```
                601                                                   650
       1  (569) AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
       3  (566) AAAAAAAAA----------------------------------------------------
       5  (569) AAAAAAAAA----------------------------------------------------
       7  (572) AAAAAAAAA----------------------------------------------------
       9  (521) AAAAAAAAA----------------------------------------------------
      11   (23) ----------------------------------------------------------
      13  (349) ----------------------------------------------------------
      15  (532) ATTCGTGACCTGATATATAANCTGYCTAATACACGGTAAAAAAAAAAAAA
      17  (522) AAA----------------------------------------------------------
      19  (521) AATCGCTATATGGTCTTTAGCCCTNCGGCGTCGTTNCACTCTNCTGGAAA
      21  (437) ----------------------------------------------------------
      23  (521) AATCGCTATATGGTCTTTAGCCCTNCGGCGTCGTTNCACTCTNCTGGAAA
Consensus (601) AAA     A
                651                                                   700
       1  (619) AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
       3  (575) ----------------------------------------------------------
       5  (578) ----------------------------------------------------------
       7  (581) ----------------------------------------------------------
       9  (530) ----------------------------------------------------------
      11   (23) ----------------------------------------------------------
      13  (349) ----------------------------------------------------------
      15  (582) AAAAAGAAAA----------------------------------------------------
      17  (525) ----------------------------------------------------------
      19  (571) NCTGGTACACTTAN----------------------------------------------
      21  (437) ----------------------------------------------------------
      23  (571) NCTGGTACACTTAN----------------------------------------------
Consensus (651)
                701
       1  (669) AAAAAAAA
       3  (575) --------
       5  (578) --------
       7  (581) --------
       9  (530) --------
      11   (23) --------
      13  (349) --------
      15  (592) --------
      17  (525) --------
      19  (585) --------
      21  (437) --------
      23  (585) --------
Consensus (701)
```

Exhibit A: Alignment of SEQ ID NOS: 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, and 23

Multiple Sequenc Alignm nt Results
(Identical amino acids are highlighted in yellow; highly conserved amino acids are highlighted in green)

Symbol comparison table: blosum62.cmp CompCheck: 1102; GapWeight: 8; GapLengthWeight: 2; 10_pileup_395059.txt MSF: 107 Type: P October 24, 2003 11:33 Check: 8204

Name: 20	Len:	107	Check: 7696	Weight:	1.00
Name: 24	Len:	107	Check: 7129	Weight:	1.00
Name: 22	Len:	107	Check: 7766	Weight:	1.00
Name: 18	Len:	107	Check: 6063	Weight:	1.00
Name: 8	Len:	107	Check: 6063	Weight:	1.00
Name: 2	Len:	107	Check: 4659	Weight:	1.00
Name: 4	Len:	107	Check: 4659	Weight:	1.00
Name: 6	Len:	107	Check: 4659	Weight:	1.00
Name: 10	Len:	107	Check: 3795	Weight:	1.00
Name: 14	Len:	107	Check: 797	Weight:	1.00
Name: 16	Len:	107	Check: 4918	Weight:	1.00

```
     1                                                        50
20 MAH QEVDYC SEEVR VGYP A...RRGCGG VQE.H VKETF VQEFDT....
24 MAH QEVDYC SEEVR VGYP A...RRGCGG VQE.H VKETF VQEFDT....
22 MAH QEVDYC SEEVR VGNP A...RRG.GG VQE.H VKETF VQEFDT....
18 MAYYQEVDYC SEEVRSVA.P AGFGRHG.GG VQQ.HVVKEKF .EEVDTVSRA
 8 MAYYQEVDYC SEEVRSVA.P AGFGRHG.GG VQQ.HVVKEKF .EEVDTVSRA
 2 MAYYQEVDYC SEEVRSVA.P AGFGRHG.GG VQQ.HVVKEKF .EEVDTVSRA
 4 MAYYQEVDYC SEEVRSVA.P AGFGRHG.GG VQQ.HVVKEKF .EEVDTVSRA
 6 MAYYQEVDYC SEEVRSVA.P AGFGRHG.GG VQQ.HVVKEKF .EEVDTVSRA
10 MAYYQEVDYC SEEVRSVA.P AGFGRHG.GG VQQ.HVVKEKF .EEVDTV RA
14 MAHYQEVDYC SEEVRSV .P TGGFLGR.GG VQQQHVVKETF .QE D...X
16 MAHYQEVDYC SEEVRSV .P TGGFLGR.GG VQQQHVVKETF .QE D...R

     51                                                      100
20 .AGRRHGHHG HHGRGSGHFE VRE R EEDI NTRTGEFHER ENF VRADD
24 .AGRRHGHHG HHGRGSGHFE VRE R EEDI NTRTGEFHER GNFS ADD
22 .GRRHGHHG HHGRGSGHFE VRE R EEDF NTRTGEFHER ENF VRADD
18 GANHHHHHHG HHG.GHG.FV VRETRVEEDI NTCTGEVHER RESFLARAN~
 8 GANHHHHHHG HHG.GHG.FV VRETRVEEDI NTCTGEVHER RESFLARAN~
 2 GAN.HHHHHG HHG.GHG.FV VRETRVEEDI NTCTGEVHER RESFLARAN~
 4 GAN.HHHHHG HHG.GHG.FV VRETRVEEDI NTCTGEVHER RESFLARAN~
 6 GAN.HHHHHG HHG.GHG.FV VRETRVEEDI NTCTGEVHER RESFLARAN~
10 GAN.HHHHHG HHG.GHG.FV VRETRVEEDI NTCTGEVHER RESFLARAN~
14 G GRXXH H. HG.NDY.X VRET XEEDF NTCTGEFRER XKELSCX PT
16 G GRHHH H. HG.NDY.L VRET VEEDF NTCTGEFRER QSFLL D~

     101
20 ~~~~~~~
24 ~~~~~~~
22 ~~~~~~~
18 ~~~~~~~
 8 ~~~~~~~
 2 ~~~~~~~
 4 ~~~~~~~
 6 ~~~~~~~
10 ~~~~~~~
14 XSNLLCV
16 ~~~~~~~
```

Exhibit B: Alignment of SEQ ID NOS: 2, 4, 6, 8, 10, 14, 16, 18, 22, and 24

Multiple Sequence Alignment Results

(Identical amino acids are highlighted in yellow)

Symbol comparison table: blosum62.cmp CompCheck: 1102

GapWeight: 8
GapLengthWeight: 2

2_pileup_394958.txt MSF: 93 Type: P October 24, 2003 11:53 Check: 1652 ..

Name: 2 Len: 93 Check: 3884 Weight: 1.00
Name: 4 Len: 93 Check: 3884 Weight: 1.00
Name: 6 Len: 93 Check: 3884 Weight: 1.00

//

```
           1                                                  50
 2 MAYYQEVDYC SEEVRSVAPA GFGRHGGGVQ QHVVKEKFEE VDTVSRAGAN
 4 MAYYQEVDYC SEEVRSVAPA GFGRHGGGVQ QHVVKEKFEE VDTVSRAGAN
 6 MAYYQEVDYC SEEVRSVAPA GFGRHGGGVQ QHVVKEKFEE VDTVSRAGAN

           51                                              93
 2 HHHHHGHHGG HGFVVRETRV EEDINTCTGE VHERRESFLA RAN
 4 HHHHHGHHGG HGFVVRETRV EEDINTCTGE VHERRESFLA RAN
 6 HHHHHGHHGG HGFVVRETRV EEDINTCTGE VHERRESFLA RAN
```

Exhibit C: Alignment of SEQ ID NOS: 2, 4, and 6